REMARKS

I. Amendments

Claims 5-12 and 17-30 are canceled. New claims 34-42 are added. Claims 1-4, 13-16, and 31-33 have been withdrawn from consideration as directed to non-elected inventions. The newly added claims do not constitute new matter and are completely supported throughout the specification and originally filed claims. More particularly, newly added claims 34-42, drawn to a transgenic mouse whose genome comprises a disruption in the endogenous mouse anaphylatoxin C3a receptor gene, a cell or tissue derived from said mouse, and a method of producing said mouse can be found, for example, at page 10, line 1 through page 16, line 22, and at page 53, line 1 through page 55, line 13, of the specification.

The foregoing amendments are made solely to expedite prosecution of the application and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, claims 34-42 are pending in the instant application.

II Rejections

A. Rejection under 35 U.S.C. § 112, first paragraph

Written Description: The Examiner has rejected claims 5-12 and 17-30 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleges that, while the specification allegedly teaches only one mouse anaphylatoxin C3a receptor gene, the claims allegedly encompass more than one anaphylatoxin C3a receptor gene, and more particularly, encompass any anaphylatoxin C3a receptor gene that may exist in each and every species of animal.

The Applicant respectfully traverses the rejection under 35 U.S.C. § 112, first paragraph. However, in light of the cancellation of claims 5-12 and 17-30, the rejection is no longer relevant, and Applicant requests withdrawal of the rejection. The Applicant submits that subject matter of new claims 34-42, drawn to a transgenic mouse whose genome comprises a disruption

in the endogenous mouse anaphylatoxin C3a receptor gene, cells and tissue obtained therefrom, and a method of making said mouse, is described in the specification in such a way as to convey possession of the invention as claimed.

Enablement: The Examiner has rejected claims 5-12 and 17-30 under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Specifically, according to the Examiner, the specification, while being enabling for a mouse or mouse cell whose genome comprises a homozygous disruption of the anaphylatoxin C3a receptor gene, wherein said mouse is a male and exhibits reduced thymus weight, thymus size or thymus to body weight ratio, or is male or female and exhibits increased susceptibility to seizure or a stimulus processing deficit, does not provide enablement for any transgenic non-human animal or a cell of any species with a disruption of any anaphylatoxin C3a receptor gene wherein said transgenic cell or animal has any phenotype.

In one aspect, the Examiner has rejected the claims based on the lack of targeted gene insertion technology available for any species other than mouse at the time of filing, and alleged lack of disclosure of any such technology in the instant specification. According to the Examiner, ES cells capable of providing germline chimeras were not available in species other than mouse.

In another aspect of the rejection, the Examiner asserts that due to the unpredictability of the phenotype of transgenic animals at the time of filing, the transgenic animal as claimed is not enabled by the specification in that it does not recite a phenotype resulting from the disruption. The Examiner also states that the specification is not enabling for a heterozygous disruption of the anaphylatoxin receptor gene in the transgenic mouse with the phenotypes as encompassed by claims 17-23, due to this unpredictability.

In another aspect of the rejection, the Examiner states that the specification fails to enable disrupting any anaphylatoxin C3a receptor gene in a mouse or any other species or a cell other than a mouse cell, due to an alleged lack of disclosure of other species of anaphylatoxin C3a receptor.

The Applicant respectfully traverses the rejection. However, the Applicant has cancelled claims 5-12 and 17-30, thus making the rejection under 35 U.S.C. § 112, first paragraph no longer relevant.

New claims 34-42 are drawn to a transgenic mouse whose genome comprises a homozygous disruption in the endogenous mouse anaphylatoxin C3a receptor gene, wherein the transgenic mouse lacks production of functional anaphylatoxin C3a receptor and exhibits reduced thymus weight, thymus size or thymus to body weight ratio, increased susceptiblity to seizure or a stimulus processing deficit when male and increased susceptiblity to seizure or a stimulus processing deficit when female, a method of making the mouse and a cell or tissue obtained therefrom. The Applicant contends that new claims 34-42 are fully enabled by the instant specification. In particular, the Applicant has described the transgenic mouse, cells and methods as claimed in the new claims 34-42 so that one skilled in the art would be apprised of how to make and use the transgenic mouse and cells and tissues as claimed.

More particularly, the genome of the transgenic mouse as presently claimed comprises a homozygous disruption in the mouse anaphylatoxin C3a receptor gene, which disruption inhibits production of the anaphylatoxin C3a receptor, resulting in a transgenic mouse exhibiting the phenotype describe above and in the instant specification. The instant specification clearly describes how to produce such a disruption in a transgenic mouse (see, for example, Figure 2 and page 53-55 of the specification) in order to create the transgenic mouse exhibiting the phenotype as claimed.

In view of the cancellation of claims 5-12 and 17-30, and the submission of new claims 34-42, which are completely enabled by the specification as originally filed as noted above, the rejection under 35 U.S.C. § 112, first paragraph, is no longer relevant. Therefore, the Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

B. Rejection under 35 U.S.C. § 103

1. Claims 5-10 were rejected under 35 U.S.C. § 103 (a) as being unpatentable over Capecchi, 1994, *Scientific American,* 270, pp34-41 ("Capecchi") in view of Tornetta, 1997, *J. Immunol.*, 158 pp 5277-5282 ("Tornetta"). The Applicant respectfully traverses this rejection. However, in view of the cancellation of claims 5-10, the rejection under 35 U.S.C. § 103 is no longer relevant.

The Applicant submits that new claims 34-42 are non-obvious over the teachings of the prior art references. More particularly, the claimed invention relates to the *in vivo* mammalian characterization of the function of the mouse anaphylatoxin C3a receptor gene, and provides transgenic mice and cells, the genomes of which comprise disruptions in the endogenous anaphylatoxin C3a receptor gene, and methods of making the mice, all of which are not obvious in view of the sole or combined teachings and disclosures of the references cited by the Examiner.

According to the Examiner, Capecchi discloses transforming a cell with a nucleic acid construct comprising a disruption in the *Hox*A-3 gene, resulting in an inactivating insertion of a selective marker gene into the endogenous *Hox*A-3 locus, and using said cell to generate a mouse whose genome comprises a disruption in the *Hox*A-3 gene.

Tornetta, as characterized by the Examiner, merely discloses the cloning of the mouse anaphylatoxin C3a receptor gene.

In order to establish a *prima facie* case of obviousness, the Examiner must meet three basic criteria: there must be some suggestion or motivation to modify a primary reference or combine reference teachings; there must be a reasonable expectation of success; and the prior art reference(s) must teach or suggest all the claim limitations. See MPEP §2143. The Applicant contends that the prior art references cited by the Examiner are not sufficient to establish a *prima facie* case of obviousness.

The Examiner asserts that the ordinary artisan would have been motivated to combine the teachings of the prior art references to determine the role of the anaphylatoxin C3a receptor gene in a mouse as it was an art-recognized goal to determine the physiological role of a gene of interest by generation of a knockout mouse. The Applicant respectfully disagrees. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. See MPEP 2143.01. However, claims 5-10 have been canceled. The Applicant submits that neither Capecchi nor Tornetta suggest the desirability of disrupting the anaphylatoxin C3a receptor gene in a mouse as presently recited in claims 34-42. Therefore, the Examiner has failed to provide sufficient evidence in the prior art references of the motivation or suggestion to combine the prior art references required to establish a case of *prima facie* obviousness.

Further, the Applicant submits that the Examiner has failed to show that one of ordinary skill in the art would have a reasonable expectation of success to make an anaphylatoxin C3a receptor knockout mouse based on the combined disclosures of the prior art references, and in particular, based on the disclosure of Capecchi, who discloses a transgenic mouse comprising a *Hox*A-3 gene disruption, and Tornetta, who provides the sequence for the mouse anaphylatoxin C3a receptor gene.

Finally, in order to establish a *prima facie* case of obviousness, the Examiner must also show that the prior art references teach or suggest all of the claimed limitations. As described above, the disclosure of Capecchi relates to a transgenic mouse having an inactivating disruption in a *Hox*A-3 gene. Tornetta is limited to providing disclosure related to the cloning of the mouse anaphylatoxin C3a receptor gene in particular.

However, neither Capecchi nor Tornetta, alone or in combination, teaches all of the limitations as presently claimed in claims 34-42. As acknowledged by the Examiner, Capecchi provides no disclosure or teaching of the anaphylatoxin C3a receptor gene described in the instant specification, and in particular does not disclose a specific phenotype of the transgenic mouse comprising a disruption in said gene, particularly a phenotype of reduced thymus weight, thymus size or thymus to body weight ratio, increased susceptibility to seizure or a stimulus processing deficit in a male and increased susceptibility to seizure or a stimulus processing deficit in a female, as claimed by the present invention. Likewise, Tornetta does not provide any teaching or suggestion relating to targeted disruptions in any gene, particularly in the mouse anaphylatoxin C3a receptor gene as presently claimed. More particularly, the disclosure of Tornetta fails to provide any teaching or suggestion that relates to the transgenic mice and cells as recited in the pending claims.

2. Claims 5-10 were also rejected under 35 U.S.C. § 103 (a) as being unpatentable over Beach, 1999, *USPN, 5,919,997* ("Beach") in view of Tornetta, 1997, *J. Immunol.*, 158 pp 5277-5282 ("Tornetta"). The Applicant respectfully traverses this rejection. However, in view of the cancellation of claims 5-10, the rejection under 35 U.S.C. § 103 is no longer relevant.

According to the Examiner, Beach discloses transforming a cell with a nucleic acid construct comprising a disruption in the INK4 gene, resulting in an inactivating insertion of a selective marker gene into the endogenous INK4 locus, and using said cell to generate a

knockout mouse whose genome comprises a disruption in the INK4 gene. Tornetta, as noted above, relates to the cloning of the mouse anaphylatoxin C3a receptor gene.

However, Beach does not teach transgenic mice or cells comprising a disruption in the anaphylatoxin C3a receptor gene as claimed by the present invention. Further, Beach does not teach the production of transgenic mice comprising disruptions in the anaphylatoxin C3a receptor gene according to the instant invention, wherein the transgenic mice exhibit the phenotype noted above and recited in claims 34-42.

Like Beach, the disclosure of Tornetta is deficient in teaching or suggesting the transgenic mouse as claimed by the present invention, and, in particular, a transgenic mouse comprising a disruption in the anaphylatoxin C3a receptor gene as currently claimed, or cells or tissue obtained from said mouse, and in particular does not disclose any teachings relating to the phenotype of such mice as claimed.

Taken together, the disclosures of Beach and Tornetta are absent of any teaching or suggestion of disrupting the anaphylatoxin C3a receptor gene of the instant invention in a mouse, and, in particular, are deficient of any teaching or suggestion of the transgenic mice, cells, tissue, and methods recited in the pending claims. More particularly, the disclosures of Beach and Tornetta, alone or in combination, do not teach or suggest in any way the transgenic mice comprising disrupted anaphylatoxin C3a receptor genes, which exhibit reduced thymus weight, thymus size or thymus to body weight ratio, increased susceptibility to seizure or a stimulus processing deficit in a male and increased susceptibility to seizure or a stimulus processing deficit in a female, methods of producing such transgenic mice, or tissues and cells obtained from such transgenic mice. For these reasons, in addition to the reasons set forth above in response to the prior obviousness rejection, claims 34-42 are not obvious in view of the prior art references.

As the obviousness rejections are no longer relevant as result of the cancellation of claims 5-10, and new claims 34-42 are not obvious in view of the teachings of Capecchi and Tornetta, and are also not obvious in view of the teachings of Beach and Tornetta, the Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. § 103.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-171.

Respectfully submitted,

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